

What is claimed:

1. An albumin fusion protein comprising a member selected from the group consisting of:
 - (a) a Therapeutic protein:X and albumin comprising the amino acid sequence of SEQ ID NO:18;
 - (b) a Therapeutic protein:X and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has albumin activity;
 - (c) a Therapeutic protein:X and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has albumin activity, and further wherein said albumin activity is the ability to prolong the shelf life of the Therapeutic protein:X compared to the shelf-life of the Therapeutic protein:X in an unfused state;
 - (d) a Therapeutic protein:X and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has albumin activity, and further wherein the fragment or variant comprises the amino acid sequence of amino acids 1-387 of SEQ ID NO:18;
 - (e) a fragment or variant of a Therapeutic protein:X and albumin comprising the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has a biological activity of the Therapeutic protein:X;
 - (f) a Therapeutic protein:X, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the N-terminus of albumin, or the N-terminus of the fragment or variant of albumin;
 - (g) a Therapeutic protein:X, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the C-terminus of albumin, or the C-terminus of the fragment or variant of albumin;
 - (h) a Therapeutic protein:X, or fragment or variant thereof, and albumin,

or fragment or variant thereof, of (a) to (e), wherein the Therapeutic protein:X, or fragment or variant thereof, is fused to the N- terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment or variant of albumin;

(i) a Therapeutic protein:X, or fragment or variant thereof, and albumin.

5 or fragment or variant thereof, of (a) to (e), which comprises a first Therapeutic protein:X, or fragment or variant thereof, and a second Therapeutic protein:X, or fragment or variant thereof, wherein said first Therapeutic protein:X, or fragment or variant thereof, is different from said second Therapeutic protein:X, or fragment or variant thereof;

(j) a Therapeutic protein:X, or fragment or variant thereof, and albumin,

10 or fragment or variant thereof, of (a) to (i), wherein the Therapeutic protein:X, or fragment or variant thereof, is separated from the albumin or the fragment or variant of albumin by a linker; and

15 (k) a Therapeutic protein:X, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (j), wherein the albumin fusion protein has the following formula:

R1-L-R2; R2-L-R1; or R1-L-R2-L-R1,

and further wherein R1 is Therapeutic protein:X, or fragment or variant thereof, L is a peptide linker, and R2 is albumin comprising the amino acid sequence of SEQ ID NO:18 or a fragment or variant of albumin.

20

2. The albumin fusion protein of claim 1, wherein the shelf-life of the albumin fusion protein is greater than the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

25

3. The albumin fusion protein of claim 1, wherein the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin, or fragment or variant thereof, is greater than the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

4. The albumin fusion protein of claim 1, wherein the in vivo biological activity
of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin, or fragment
or variant thereof, is greater than the in vivo biological activity of the Therapeutic
5 protein:X, or fragment or variant thereof, in an unfused state.

5. An albumin fusion protein comprising a Therapeutic protein:X, or fragment
or variant thereof, inserted into an albumin, or fragment or variant thereof, comprising the
amino acid sequence of SEQ ID NO:18 or fragment or variant thereof.

10

6. An albumin fusion protein comprising a Therapeutic protein:X, or fragment
or variant thereof, inserted into an albumin, or fragment or variant thereof, comprising an
amino acid sequence selected from the group consisting of:

- (a) amino acids 54 to 61 of SEQ ID NO:18;
- 15 (b) amino acids 76 to 89 of SEQ ID NO:18;
- (c) amino acids 92 to 100 of SEQ ID NO:18;
- (d) amino acids 170 to 176 of SEQ ID NO:18;
- (e) amino acids 247 to 252 of SEQ ID NO:18;
- (f) amino acids 266 to 277 of SEQ ID NO:18;
- 20 (g) amino acids 280 to 288 of SEQ ID NO:18;
- (h) amino acids 362 to 368 of SEQ ID NO:18;
- (i) amino acids 439 to 447 of SEQ ID NO:18;
- (j) amino acids 462 to 475 of SEQ ID NO:18;
- (k) amino acids 478 to 486 of SEQ ID NO:18; and
- 25 (l) amino acids 560 to 566 of SEQ ID NO:18.

7. The albumin fusion protein of claim 5, wherein said albumin fusion protein
comprises a portion of albumin sufficient to prolong the shelf-life of the Therapeutic

protein:X, or fragment or variant thereof, as compared to the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

8. The albumin fusion protein of claim 6, wherein said albumin fusion protein
5 comprises a portion of albumin sufficient to prolong the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, as compared to the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

9. The albumin fusion protein of claim 5, wherein said albumin fusion protein
10 comprises a portion of albumin sufficient to prolong the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin as compared to the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

15 10. The albumin fusion protein of claim 6, wherein said albumin fusion protein
comprises a portion of albumin sufficient to prolong the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin as compared to the in vitro biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

20 11. The albumin fusion protein of claim 5 wherein said albumin fusion protein
comprises a portion of albumin sufficient to prolong the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, fused to albumin compared to the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an
25 unfused state.

12. The albumin fusion protein of claim 6 wherein said albumin fusion protein
comprises a portion of albumin sufficient to prolong the in vivo biological activity of the

Therapeutic protein:X, or fragment or variant thereof, fused to albumin compared to the in vivo biological activity of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

5 13. The albumin fusion protein of any one of claims 1-12, which is non-glycosylated.

10 14. The albumin fusion protein of any one of claims 1-12, which is expressed in yeast.

15 15. The albumin fusion protein of claim 14, wherein the yeast is glycosylation deficient.

20 16. The albumin fusion protein of claim 14 wherein the yeast is glycosylation and protease deficient.

25 17. The albumin fusion protein of any one of claims 1-12, which is expressed by a mammalian cell.

18. The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein is expressed by a mammalian cell in culture.

19. The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein further comprises a secretion leader sequence.

20. A composition comprising the albumin fusion protein of any one of claims 1-12 and a pharmaceutically acceptable carrier.

21. A kit comprising the composition of claim 20.

22. A method of treating a disease or disorder in a patient, comprising the step of administering the albumin fusion protein of any one of claims 1-12.

5

23. The method of claim 22, wherein the disease or disorder comprises indication:Y.

24. A method of treating a patient with a disease or disorder that is modulated by Therapeutic protein:X, or fragment or variant thereof, comprising the step of administering an effective amount of the albumin fusion protein of any one of claims 1-12.

10 25. The method of claim 24, wherein the disease or disorder is indication:Y.

15 26. A method of extending the shelf life of Therapeutic protein:X, or fragment or variant thereof, comprising the step of fusing the Therapeutic protein:X, or fragment or variant thereof, to albumin, or fragment or variant thereof, sufficient to extend the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, compared to the shelf-life of the Therapeutic protein:X, or fragment or variant thereof, in an unfused state.

20

27. A nucleic acid molecule comprising a polynucleotide sequence encoding the albumin fusion protein of any one of claims 1-12.

25 28. A vector comprising the nucleic acid molecule of claim 27.

29. A host cell comprising the nucleic acid molecule of claim 28.

30. An albumin fusion protein comprising a member selected from the group

consisting of:

- (a) an IL-2 and albumin comprising the amino acid sequence of SEQ ID NO:18;
- (b) an IL-2 and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has albumin activity;
- (c) an IL-2 and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has albumin activity, and further wherein said albumin activity is the ability to prolong the shelf life of the IL-2 compared to the shelf-life of the IL-2 in an unfused state;
- 10 (d) an IL-2 and a fragment or a variant of the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has albumin activity, and further wherein the fragment or variant comprises the amino acid sequence of amino acids 1-387 of SEQ ID NO:18;
- 15 (e) a fragment or variant of an IL-2 and albumin comprising the amino acid sequence of SEQ ID NO:18, wherein said fragment or variant has T cell proliferative activity or T cell activation activity;
- (f) an IL-2, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), wherein the IL-2, or fragment or variant thereof, is fused to the N-terminus of albumin, or the N-terminus of the fragment or variant of albumin;
- 20 (g) an IL-2, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), wherein the IL-2, or fragment or variant thereof, is fused to the C-terminus of albumin, or the C-terminus of the fragment or variant of albumin;
- (h) an IL-2, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), wherein the IL-2, or fragment or variant thereof, is fused to the N-terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment or variant of albumin;
- 25 (i) an IL-2, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (e), which comprises the IL-2, or fragment or variant thereof, and a

Therapeutic protein:X, or fragment or variant thereof, wherein said IL-2, or fragment or variant thereof, is different from said second Therapeutic protein:X, or fragment or variant thereof;

5 (j) an IL-2, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (i), wherein the IL-2, or fragment or variant thereof, is separated from the albumin or the fragment or variant of albumin by a linker; and

(k) an IL-2, or fragment or variant thereof, and albumin, or fragment or variant thereof, of (a) to (j), wherein the albumin fusion protein has the following formula:

R1-L-R2; R2-L-R1; or R1-L-R2-L-R1,

10 and further wherein R1 is IL-2, or fragment or variant thereof, L is a peptide linker, and R2 is albumin comprising the amino acid sequence of SEQ ID NO:18 or a fragment or variant of albumin.

15 31. The albumin fusion protein of claim 30, wherein the shelf-life of the albumin fusion protein is greater than the shelf-life of the IL-2, or fragment or variant thereof, in an unfused state.

20 32. The albumin fusion protein of claim 30, wherein the in vitro T cell proliferative activity or T cell activation activity of the IL-2, or fragment or variant thereof, fused to albumin, or fragment or variant thereof, is greater than the in vitro T cell proliferative activity or T cell activation activity of the IL-2, or fragment or variant thereof, in an unfused state.

25 33. The albumin fusion protein of claim 30, wherein the in vivo T cell proliferative activity or T cell activation activity of the IL-2, or fragment or variant thereof, fused to albumin, or fragment or variant thereof, is greater than the in vivo T cell proliferative activity or T cell activation activity of the IL-2, or fragment or variant thereof, in an unfused state.

34. An albumin fusion protein comprising an IL-2, or fragment or variant thereof, inserted into an albumin, or fragment or variant thereof, comprising the amino acid sequence of SEQ ID NO:18 or fragment or variant thereof.

5

35. An albumin fusion protein comprising an IL-2, or fragment or variant thereof, inserted into an albumin, or fragment or variant thereof, comprising an amino acid sequence selected from the group consisting of:

- (a) amino acids 54 to 61 of SEQ ID NO:18;
- (b) amino acids 76 to 89 of SEQ ID NO:18;
- (c) amino acids 92 to 100 of SEQ ID NO:18;
- (d) amino acids 170 to 176 of SEQ ID NO:18;
- (e) amino acids 247 to 252 of SEQ ID NO:18;
- (f) amino acids 266 to 277 of SEQ ID NO:18;
- (g) amino acids 280 to 288 of SEQ ID NO:18;
- (h) amino acids 362 to 368 of SEQ ID NO:18;
- (i) amino acids 439 to 447 of SEQ ID NO:18;
- (j) amino acids 462 to 475 of SEQ ID NO:18;
- (k) amino acids 478 to 486 of SEQ ID NO:18; and
- (l) amino acids 560 to 566 of SEQ ID NO:18.

10

15

20

25

36. The albumin fusion protein of claim 34, wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the shelf-life of the IL-2, or fragment or variant thereof, as compared to the shelf-life of the IL-2, or fragment or variant thereof, in an unfused state.

37. The albumin fusion protein of claim 35, wherein said albumin fusion protein comprises a portion of albumin sufficient to prolong the shelf-life of the IL-2, or fragment or

variant thereof, as compared to the shelf-life of the IL-2, or fragment or variant thereof, in an unfused state.

38. The albumin fusion protein of claim 34, wherein said albumin fusion protein
5 comprises a portion of albumin sufficient to prolong the in vitro T cell proliferative activity
or T cell activation activity of the IL-2, or fragment or variant thereof, fused to albumin as
compared to the in vitro T cell proliferative activity or T cell activation activity of the IL-2,
or fragment or variant thereof, in an unfused state.

10 39. The albumin fusion protein of claim 35, wherein said albumin fusion protein
comprises a portion of albumin sufficient to prolong the in vitro T cell proliferative activity
or T cell activation activity of the IL-2, or fragment or variant thereof, fused to albumin as
compared to the in vitro T cell proliferative activity or T cell activation activity of the IL-2,
or fragment or variant thereof, in an unfused state.

15 40. The albumin fusion protein of claim 34 wherein said albumin fusion protein
comprises a portion of albumin sufficient to prolong the in vivo T cell proliferative activity
or T cell activation activity of the IL-2, or fragment or variant thereof, fused to albumin
compared to the in vivo T cell proliferative activity or T cell activation activity of the IL-2,
20 or fragment or variant thereof, in an unfused state.

41. The albumin fusion protein of claim 35 wherein said albumin fusion protein
comprises a portion of albumin sufficient to prolong the in vivo T cell proliferative activity
or T cell activation activity of the IL-2, or fragment or variant thereof, fused to albumin
25 compared to the in vivo T cell proliferative activity or T cell activation activity of the IL-2,
or fragment or variant thereof, in an unfused state.

42. The albumin fusion protein of any one of claims 30-41, which is non-

glycosylated.

43. The albumin fusion protein of any one of claims 30-41, which is expressed in yeast.

5

44. The albumin fusion protein of claim 43, wherein the yeast is glycosylation deficient.

10 45. The albumin fusion protein of claim 43 wherein the yeast is glycosylation and protease deficient.

46. The albumin fusion protein of any one of claims 30-41, which is expressed by a mammalian cell.

15 47. The albumin fusion protein of any one of claims 30-41, wherein the albumin fusion protein is expressed by a mammalian cell in culture.

48. The albumin fusion protein of any one of claims 30-41, wherein the albumin fusion protein further comprises a secretion leader sequence.

20

49. A composition comprising the albumin fusion protein of any one of claims 30-41 and a pharmaceutically acceptable carrier.

50. A kit comprising the composition of claim 49.

25

51. A method of treating a disease or disorder in a patient, comprising the step of administering the albumin fusion protein of any one of claims 30-41.

52. The method of claim 51, wherein the disease or disorder comprises a member selected from the group consisting of: metastatic renal cell carcinoma; metastatic melanoma; malignant melanoma; renal cell carcinoma; HIV infection; inflammatory bowel disorder; Kaposi's sarcoma; leukaemia; multiple sclerosis; rheumatoid arthritis; transplant rejection; 5 type 1 diabetes mellitus; lung cancer; acute myeloid leukaemia; hepatitis C; non-hodgkin's lymphoma; and ovarian cancer.

53. A method of treating a patient with a disease or disorder that is modulated by IL-2, or fragment or variant thereof, comprising the step of administering an effective 10 amount of the albumin fusion protein of any one of claims 30-41.

54. The method of claim 53, wherein the disease or disorder comprises a member selected from the group consisting of: metastatic renal cell carcinoma; metastatic melanoma; malignant melanoma; renal cell carcinoma; HIV infection; inflammatory bowel disorder; 15 Kaposi's sarcoma; leukaemia; multiple sclerosis; rheumatoid arthritis; transplant rejection; type 1 diabetes mellitus; lung cancer; acute myeloid leukaemia; hepatitis C; non-hodgkin's lymphoma; and ovarian cancer.

55. A method of extending the shelf life of IL-2, or fragment or variant thereof, 20 comprising the step of fusing the IL-2, or fragment or variant thereof, to albumin, or fragment or variant thereof, sufficient to extend the shelf-life of the IL-2, or fragment or variant thereof, compared to the shelf-life of the IL-2, or fragment or variant thereof, in an unfused state.

25 56. A nucleic acid molecule comprising a polynucleotide sequence encoding the albumin fusion protein of any one of claims 30-41.

57. A vector comprising the nucleic acid molecule of claim 56.

58. A host cell comprising the nucleic acid molecule of claim 57.

59. An albumin fusion protein comprising albumin, or a fragment or variant
5 thereof, and a protein selected from the group consisting of:

- (a) calcitonin;
- (b) growth hormone releasing factor;
- (c) IL-2 fusion protein;
- (d) insulin-like growth factor-1;
- 10 (e) interferon beta; and
- (f) parathyroid hormone.